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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,824	08/09/2001	Christopher K. Murphy	15132-292001/ MPI2000-314	4663

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EXAMINER	
VOGEL, NANCY S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,824	MURPHY, CHRISTOPHER K.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) 20-25 and 29-35 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,4-11,14-18 and 26-28 is/are rejected.

7)☒ Claim(s) 2,3,12,13 and 19 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 09 August 2001 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/17/03, 3/4/02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-35 are pending in the case

Receipt of Information Disclosure Statements on 3/17/03, and 3/4/02, is acknowledged.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-18, and 26-28 in the reply filed on 11/23/04 is acknowledged.

Claims 20-26, and 29-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/23/04.

Claim Objections

Claims 2, 12 and 19 are objected to because of the following informalities: The claims recite the phrase "wherein the promoter is *panB*". Since "*panB*" refers to the gene including the encoded enzyme, it would be more clear if applicants recited "the *panB* promoter". Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1, 4-11, 14-18, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claims 1, 9, 14, 27 and 28, and by dependence, claims 4-8, 10-11, 15-18, are drawn to a method of determining whether a test compound is an inhibitor of bacterial tetrahydrofolate biosynthesis, or an antibacterial agent, comprising measuring activity of a promoter, the activity of which is increased in the presence of a compound that inhibits tetrahydrofolate biosynthesis, and further formulating the selected compound as an inhibitor or antibacterial agent (claims 27 and 28).

Claims 1, 4-11, 14-18, 27 and 28 are genus claims in terms of a method using any promoter, whose activity is increased in the presence of a compound that inhibits tetrahydrofolate biosynthesis. The claims encompass a broad class of methods using a promoter that may be virtually any promoter that has this function. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods utilizing the encompassed promoters based on the teachings of the

specification. While the specification provides information on the structure of the *B. subtilis panB* promoter, there is no disclosure of the precise structure of a promoter useful for identifying compounds which inhibit bacterial tetrahydrofolate biosynthesis, or with antibacterial activity. Furthermore, there is no structure-function analysis of the disclosed *B. subtilis panB* promoter to provide guidance on the essential regions of promoter, i.e. those regions responsible for the increased activity in the presence of inhibitors of tetrahydrofolate biosynthesis. Therefore, the specification does not describe the claimed method utilizing promoters which have increased activity in the presence of a compound that inhibits tetrahydrofolate activity, in such clear, concise and exact terms so as to indicate that Applicant had possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

Claim 26 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims any composition comprising an antibacterial agent identified by the method of claim 14 and a pharmaceutically acceptable carrier. Claim 14 is drawn to a method of determining whether a test compound is an antibacterial agent, by measuring the response of any promoter whose activity is increased in the presence of

a compound that inhibits tetrahydrofolate biosynthesis, linked to a reporter gene. The claim reads on a broad genus of antibacterial agents with a particular function, i.e. the ability to kill or inhibit the growth of bacteria, and which increase the activity of a promoter whose activity is increased in the presence of a compound that inhibits tetrahydrofolate biosynthesis.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims any composition comprising an antibacterial agent which increases the activity of a promoter which is increased in the presence of a compound that inhibits a tetrahydrofolate biosynthesis, without disclosing any structural information regarding these products. The specification provides only general teachings regarding the structure of the antibacterial agents, stating that "test compounds can be any compound, such as a small organic or inorganic molecule, amino acid, polypeptide, nucleic acid, peptide nucleic acid, carbohydrate, or polysaccharide. The test compounds can be synthetic, naturally occurring, or a combination of synthetic and natural

components. If desired, the test compound can be a member of a library of test compounds (e.g., a combinatorial chemical library) or a component of a cellular extract or bodily fluid (e.g., urine, blood, tears, sweat, or saliva)" (page 8 of the specification). The specification provides no structural or specific functional characteristics of antibacterial agents. Because the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification, the instant specification has not satisfied the written description for the claimed genus. The recitation in the claims and specification of antibacterial compositions which are waiting to be discovered, does not satisfy the written description requirement.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one of skill in the art to envision a representative number of antibacterial compositions having the recited activity. Thus, the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Claim 26 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include,

but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Nature of the invention: The instant claim is drawn to compositions comprising an antibacterial agent which is identified by a method comprising contacting a bacterial cell which comprises a promoter whose activity is increased in the presence of a compound that inhibits tetrahydrofolate biosynthesis operably linked with a reporter gene, with said agent. The specification teaches that said compositions can be used to treat bacterial infection. The claim encompasses products that are not described in the specification, and indeed may not have been identified anywhere. Thus the invention encompasses "reach-through" claims that attempt to gain patent coverage for subject matter that cannot be made in view of the instant specification alone. It is noted specifically that the ability to "identify" is not equivalent to the ability to "make and "use', which is the standard for meeting the enablement requirement.

Scope of the art: The scope of the invention is very broad, encompassing any molecule having the ability to inhibit the growth of, or kill, bacteria, and which increase the activity of a promoter whose activity is increased in the presence of a compound that inhibits tetrahydrofolate biosynthesis. This includes molecules that have not been identified or described in the specification (or anywhere).

The state of the prior art, and the predictability or unpredictability of the art: The claim as drafted comprises any molecule, including nucleic acids, which can act to increase the activity of particular promoters in bacterial cells. There is much unpredictability in the field of designing agents which will activate a promoter in a bacterial cell. For instance, regarding the use of nucleic acids such as antisense molecules (which is one molecule possibly encompassed by the claim whose general structural nature, although not particular structure, can be envisioned), Branch (TIBS Vol. 23, pp. 45-50, 1998) teaches, e.g. as summarized in the Abstract, that there was no clear demonstration of an antisense molecule acting as an antisense agent against the intended single target gene as of that date. Clearly, use of antisense agents was far from routine. Branch also shows that mere knowledge of a potential target gene does not predict that an antisense would actually function as planned, and that its design was far from routine in the art. Therefore, such agents was not able to routinely made by one of ordinary skill in the art at the time of filing.

The amount of direction or guidance presented in the specification, and the presence or absence of working examples: The specification has presented no direction or guidance for the isolation of antimicrobials, other than setting forth a general screening method involving high through-put techniques using the claimed methods. There are no working examples of such methods using candidate substances. Furthermore, there are no working examples concerning how to use the claimed products. There is no teaching, other than general statements regarding possible formulations and modifications which may be necessary for pharmaceutical

effectiveness (pages 11-14), regarding how to administer the claimed compositions so as to effect treatment of bacterial infections.

In summary, the claims fail to meet the enablement requirement for the "how to make" and the "how to use" prong of 35 USC 112 p.1, since (1) the instant fact pattern files to disclose any particular structure for the claimed antibacterial agent; the specification does not provide sufficient guidance or working examples in this unpredictable art, and thus the artisan would have been unable to have prepared the claimed antagonist without undue experimentation, and (2) the specification does not teach how to administer the claimed antibacterial agents so as to effect a viable treatment for bacterial infection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Rohlman et al. (J. Bacter. 172, 12, pp.7200-7210, 1990).

Rohlman et al. disclose a method comprising contacting a bacterial cell with a test compound, wherein the bacterial cell contains a promoter, the activity of which is increased in the presence of a compound that inhibits tetrahydrofolate biosynthesis, and

measuring the activity of the promoter. The reference teaches the measurement of activity of the promoters in the cell after treatment with an inhibitor of bacterial tetrahydrofolate biosynthesis, i.e. trimethoprim, by examining the patterns of protein expression induced by treatment of the strain with trimethoprim in a two-dimensional electrophoretic resolution of the total cellular proteins (see Fig. 3, abstract and page 7206, right column, first complete paragraph – page 7207).

Claim 26 is rejected under 35 U.S.C. 102(b) as being anticipated by Tan et al. (EP 0 200 252) (cited by applicants).

Tan et al. disclose a composition comprising an antibacterial agent which is trimethoprim and a pharmaceutically acceptable carrier (see abstract, and page 1). It is noted that when a bacterial cell which is B. subtilis is contacted with trimethoprim, the activity of the panB promoter is increased, as taught at page 15-16 of the instant specification.

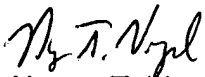
Claims 3 and 13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nancy T. Vogel
Patent Examiner